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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,755	03/09/2001	Seth A. Darst	IPT-012.01	8223

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EXAMINER
LY, CHEYNE D

ART UNIT	PAPER NUMBER
1631	15

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,755	DARST ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/12/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *1-26 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-30* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 November 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7,12,14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election with traversal of Group VIII, claims 27-29, Species A (bacterial RNA polymerase), in Paper No. 10, filed August 12, 2002, is acknowledged.

2. The traversal is on the ground(s) that it would not be unduly burdensome to perform a search on claims 1-30 together. This is not found persuasive because nucleic acids and polypeptides are directed to different chemical types regarding the critical limitations therein. Further, the distinct methods of use corresponding to each chemical type support the undue search burden if they were examined together. While taking advantage of the distinct properties of each chemical type, these usages have distinct goals as requiring distinct and different functions and results thereof without overlapping search due to different subject matter. This lack of overlapping searches documents the undue search burden if they were search together.

3. Further, Applicant traverses on the ground(s) neither of the claims in Group VIII recites "bacterial" or "eukaryotic" and no undue burden would be required to search all groups. This is not found persuasive because bacterial is recited throughout the selected claims (claim 27, lines 2 and step (b), claim 28, step (c) and (d), and claim 29, step (e) and (f)) of Group VIII. "eukaryotic" is recited in claim 29, step (e) and (f). Each species of Group VIII is distinct because each adds a feature to the method of identifying of compounds with different and distinct functions and each would require a separate and burdensome search for the basic detection compounds (See Paper No. 9, mailed June 7, 2002, Page 11).

4. The requirement is still deemed proper and is therefore made FINAL.

5. Claims 27-29 are examined on the merits.

IDS

6. Document EP listed in Paper No. 12, filed October 1, 2002, has not been considered because the listed document is an International Search Report, which does not have a publication date as is required for consideration for a reference listed on a PTO Form 1449. Further, document EU listed in Paper 14, filed November 12, 2002, has not been considered because the listed document does not have a publication date on the PTO Form 1449 as is required for consideration for a reference.

Provisional Obvious-Type Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

8. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

9. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 27-29 are rejected under the judicially created doctrine of double patenting over claims 7 and 8 of U. S. Patent No. US006225076B1, since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

11. Claims 7 and 8 of U. S. Patent No. US006225076B1 claim a method of identifying an agent that inhibits bacterial growth comprising:

12. (a) selecting a potential agent by performing rational drug design with the set of atomic coordinates in Table 3, wherein said selecting is performed in conjunction with computer modeling;

13. (b) contacting the potential agent with a bacterial culture; and

14. (c) measuring the growth of the bacterial culture under conditions in which the bacterial culture grows in the absence of the agent; wherein a potential agent is identified as an agent that inhibits bacterial growth when there is a decrease in the growth of the bacterial culture in the presence of the agent relative to in its absence.

15. (d) contacting the agent with a eukaryotic cell; and

16. (e) measuring the amount of proliferation of the eukaryotic cell under conditions in which the eukaryotic cell proliferates in the absence of the agent; wherein an agent is identified as an agent for inhibiting bacterial growth when there is no change in the proliferation of the eukaryotic cell in the presence of the agent relative to in its absence; and wherein the agent identified inhibits bacterial growth but not eukaryotic proliferation.

17. Even though claims 7 and 8 of U. S. Patent No. US006225076B1 do not specify that the atomic coordinates be derived from a rifampicin bound RNA polymerase, the specification

discloses "[i]nitially, compounds known to bind bacterial RNA polymerase, for example rifampicin which binds to the .beta. subunit, can be systematically modified by computer modeling programs until one or more promising potential analogs are identified. In addition systematic modification of selected analogs can then be systematically modified by computer modeling programs until one or more potential analogs are identified" (Column 22, lines 1-8). Further, "[a] potential inhibitor (e.g., a candidate drug) would be expected to interfere with bacterial growth (Column 24, lines 52-55). "The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent" (MPEP § 804 (II) (B) (1)).

CLAIM REJECTIONS 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Darst et al. (US006225076B1) in view of In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983).

21. Darst et al. discloses "a method of identifying an agent that inhibits bacterial growth comprising:

22. (a) selecting a potential agent by performing rational drug design with the set of atomic coordinates in Table 3, wherein said selecting is performed in conjunction with computer modeling;

23. (b) contacting the potential agent with a bacterial culture; and

24. (c) measuring the growth of the bacterial culture under conditions in which the bacterial culture grows in the absence of the agent; wherein a potential agent is identified as an agent that inhibits bacterial growth when there is a decrease in the growth of the bacterial culture in the presence of the agent relative to in its absence.

25. (d) contacting the agent with a eukaryotic cell; and

26. (e) measuring the amount of proliferation of the eukaryotic cell under conditions in which the eukaryotic cell proliferates in the absence of the agent; wherein an agent is identified as an agent for inhibiting bacterial growth when there is no change in the proliferation of the eukaryotic cell in the presence of the agent relative to in its absence; and wherein the agent identified inhibits bacterial growth but not eukaryotic proliferation." (Claims 7 and 8).

27. Even though the method disclosed by Darst et al. does not specify that the atomic coordinates be derived from rifampicin bound to the core RNA polymerase (Rif-RNAP), the specific limitations of atomic coordinates of rifampicin bound to the core RNA polymerase in this instant case do not distinguish the invention from the prior art in term of patentability because they are descriptive nonfunctional subject matter.

28. In re Gulack defines nonfunctional descriptive material, as when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the invention from the prior art in term of patentability. Also, the MPEP indicates that descriptive material that cannot exhibit any functional interrelationship with the way in which computing processes are performed does not constitute a statutory process, machine, manufacture or composition (MPEP § 2106 (IV)(B)(b)).

29. In addition, Darst et al. discloses, "[i]nitially, compounds known to bind bacterial RNA polymerase, for example rifampicin which binds to the .beta. subunit, can be systematically modified by computer modeling programs until one or more promising potential analogs are identified. In addition systematic modification of selected analogs can then be systematically modified by computer modeling programs until one or more potential analogs are identified" (Column 22, lines 1-8). "In the presence of rifampicin, RNAP forms the open complex on promoter DNA and initiates RNA synthesis, but elongation of the RNA product halts after only a few nucleotides. Elongating RNAP, however, is resistant to rifampicin. These properties have led to the idea that the presence of rifampicin inhibits RNA synthesis by blocking the path of the elongating RNA" (Column 34, lines 50-52). Further, "[a] potential inhibitor (e.g., a candidate

drug) would be expected to interfere with bacterial growth. Therefore, an assay that can measure bacterial growth may be used to identify a candidate drug" (Column 24, lines 52-55).

30. Clearly, a skilled artisan would have been motivated to partake the concept emphasized by Darst et al. for a method of identifying a compound that is predicted to inhibit bacterial growth. Darst et al. also teaches compounds such as rifampicin which bind to RNA polymerase could be model to identify analogs (Column 22, lines 1-8) and "[a] potential inhibitor (e.g., a candidate drug) would be expected to interfere with bacterial growth" (Column 24, lines 52-55). Further, the critical limitation of atomic coordinates of rifampicin bound to the core RNA polymerase is regarded as nonfunctional descriptive material as defined by In re Gulack. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the method of Darst et al. for identifying a compound that is predicted to inhibit bacterial growth.

LACK OF ENABLEMENT UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

31. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

32. Claims 27-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal core RNA polymerase with rifampicin which have atom coordinates instantly disclosed, does not reasonably provide enablement for a crystal of a portion of the core RNA polymerase with rifampicin. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

33. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

34. It is acknowledged that the applicant has disclosed information to enable one skilled in the art to make a crystal of core RNA polymerase with rifampicin (Pages 52-55). However, claims 27-29 are drawn to a method of identifying a compound that inhibits bacterial growth based on the structure of rifampicin bound to a portion of the core RNA polymerase. It is well documented that protein crystallization is in essence a trial-and-error method, and the results are usually unpredictable (Drenth, J.). Further, as recently as November 1, 2002, Science published a *New Focus* article depicting the current state of the art for protein crystallization that supports the unpredictability of the art. In essence, protein crystallization is still a trial and error process because the current technology for producing protein for the crystallization process is unpredictable, which results in high failure rate for proteins that are being crystallized.

Therefore, researchers continue to have trouble generating sufficient protein required for the crystallization process (Science, 2002). In light of the difficulty of the protein crystallization process, it is, therefore, unreasonable to expect one skilled in the art to use the information disclosed for one specific crystal to make other of predictable quality that are different from the crystal disclosed in the specification without undue experimentation. Specific to the core RNA polymerase with rifampicin, it is unlikely for one skilled in the art to use the information disclosed for one specific crystal to make others of predictable quality where the crystal is of a portion of the core RNA polymerase with rifampicin.

CONCLUSION

35. No claim is allowed.

36. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

37. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

38. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

39. Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
1/19/03

Ardin H. Marschel

ARDIN H. MARSCHEL
PRIMARY EXAMINER